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ULTRASOUND MOLECULAR IMAGING OF THROMBOSIS USING AN ACTIVATED PLATELET TARGETED MICROBUBBLES IN AN ARACHIDONIC ACID MOUSE MODEL

ACC Poster Contributions
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Session Title: Novel Applications of Contrast Echocardiography
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Background: Activated platelets initiate thrombus formation in atherosclerotic diseases has been linked to serious clinical events. Molecular imaging of activated platelet could be valuable to identify high-risk plaques before the onset of clinical events. We hypothesized that microbubbles targeted to activated platelet with contrast-enhanced ultrasound (CEU) could noninvasive in vivo visualization of thrombus formation to identify vulnerable atherosclerotic plaques.

Methods: Thrombus was induced in 18 C57BL/6 mice via topical application of arachidonic acid (AA) on the carotid. Thrombus formation was imaged with intravital fluorescence microscopy using calcein AM incubated platelets. Targeted microbubbles to glycoprotein $\alpha IIb\beta 3$, which is over-expressed on activated platelets, were modified covalently with cyclic RGD peptide (MBRGD). Control microbubbles were conjugated with nonspecific peptide (MBCON). Flow chamber studies were performed to assess attachment of MBRGD and MBCON to glycoprotein $\alpha IIb\beta 3$ (shear stress 2dyn/cm2). In vivo CEU imaging was performed at 15 minutes after microbubbles injection. The contralateral carotid with sham surgery served as control.

Results: Fluorescence microscopy confirmed that activated platelets immediately started adhering arterial wall after AA application. Thrombus in the AA treated artery was clearly noted by histology but not in the control artery. In flow chamber experiments, there was 4-folds greater attachment of MBRGD to the glycoprotein $\alpha IIb\beta 3$ as compared to MBCON ($P<0.05$). There were significant differences in VI of the MBRGD between thrombotic and sham surgery carotid artery (17.5 ± 3.3 vs 3.2 ± 1.6, $P<0.05$) at 15 minutes after microbubbles injection. As expected, VI of the MBRGD was significantly higher than that of MBCON (17.5 ± 3.3 vs 7.1 ± 2.4, $P<0.05$) in thrombotic carotid artery.

Conclusions: Activated platelet can be detected by CEU molecular imaging with microbubbles targeted to glycoprotein $\alpha IIb\beta 3$. Target-specific CEU imaging of activated platelet may be useful for non-invasive detection of high risk and vulnerable atherosclerotic plaques.